89 **GENOTOXIC EFFECTS OF NICKEL MONOARSENIDE AND NICKEL SUBARSENIDE IN THE SOMATIC WING SPOT ASSAY OF DROSOPHILA.** Katz AJ[1], Chiu A[2], Chiu N[3], Beaubier J[2], Shi X[4]. [1]Department of Biological Sciences, Illinois State University, Normal, IL 61761. [2]Office of Research and Development, U.S. EPA, Washington, DC 20460. [3]Office of Science and Technology, U.S. EPA, Washington, DC 20460. [4]Pathology and Physiology Research Branch, NIOSH, Morgantown, WV 26505.

Two nickel arsenide compounds, nickel monoarsenide (NiAs) and nickel subarsenide ($Ni_5As_2$), were evaluated for genotoxicity in the somatic wing spot assay of *Drosophila melanogaster*. Both compounds were evaluated at 80 mM in a 6-hr acute feeding exposure involving third instar larvae trans-heterozygous for the marker genes *mwh* (multiple wing hair) and *flr* (flare). All treatments were performed at 25°C. Both compounds were found to be positive inducers ($p<0.05$) of small single spots on the adult wing blade in comparison to negative control wings. However, neither compound was found to induce either large single spots or twin spots. These results are nearly identical to those observed previously for NiO-black in the wing spot assay. Twin spots in the assay arise exclusively from mitotic recombination events occurring between the *flr* locus and the centromere. Nickel has previously been implicated in the spreading of heterochromatic regions in the genome via chromatin condensation. Hence, the inability of these three genotoxic nickel compounds to induce twin spots may be due in part to Ni-induced spreading of the heterochromatic regions surrounding the centromere.

90 **GENE EXPRESSION PATTERNS IN HUMAN LIVER CELLS EXPOSED TO TETRACHLOROETHYLENE AND ITS METABOLITE USING MICROARRAY ANALYSIS.** Keshava N[1], Ong T[1]. [1]Toxicology and Molecular Biology Branch, National Institute for Occupational Safety and Health, Morgantown, WV 26505.

Occupational exposure to tetrachloroethylene (TCE) occurs through inhalation, skin contact or ingestion during its use in dry cleaning and degreasing. Tetrachloroacetic acid (TCA), a major end metabolite of TCE, has been reported in human blood and urine after exposure to TCE. In our laboratory, studies have been conducted to determine changes in gene expression patterns in cultured human cells exposed to TCE and TCA. Exponentially growing normal human liver cells were treated with 200 and 400 µM of TCE or TCA for 12h. Total RNA was used for the preparation of double stranded cDNA. Biotin labeled cRNA transcripts were synthesized, fragmented and hybridized to HuGeneFL GeneChip probe arrays representing more than 6800 human genes and expressed sequence tags. The arrays were stained with streptavidin-phycoerythrin and biotinylated anti-streptavidin antibodies. The differential gene expression data analysis was performed using GeneChip 4.0 software. Altered gene expression was observed in atleast 35 genes with a 2 fold or more change in both TCE and TCA-exposed group. Significantly higher expression was observed in tumor necrosis factor receptor in the TCA treatment group compared to the parent compound - TCE. Similarly, expression of heat shock protein 70 increased 8.8 fold in TCA treatment group compared to TCE treatment which had 2.7 fold increase. However, certain genes such as elongation factor1 delta, initiation factor 2B-$^a$, m-phase phosphoprotein had a marginal increase in response to both TCE and TCA compared to control group. These results indicate that metabolite compound preferentially affects certain set of genes. Whether difference in the expression patterns of these genes is associated with difference in carcinogenic potential of TCE and/or TCA needs to be elucidated.

91 **ASSOCIATION OF ALDH2 POLYMORPHISM WITH ACETALDEHYDE-INDUCED MICRONUCLEI AND FACIAL FLUSHING AFTER ALCOHOL INTAKE.** Kim JS[1], Cho YH[1], Kim YJ[1], Kim TY[1], Chung HW[1]. [1]School of Public Health, Seoul National University, 28 Yun keun-dong, Chongro-Ku, Seoul, 110-460, Korea.

In order to investigate whether the induction of micronuclei by acetaldehyde is associated with genetic polymorphisms of Aldehyde dehydrogenease-2(ALDH2) gene, the cytokinesis-block micronucleus (CBMN) assay in 47 human lymphocytes exposed *in vitro* to acetaldehyde were performed. The facial flushing due to alcohol intake was analysed for the association with ALDH2 gene polymorphism. Frequency of acetaldehyde induced micronuclei increased in a dose-dependent manner($p<0.05$). The distribution of $ALDH2^1/ALDH2^1$, $ALDH2^1/ALDH2^2$ and $ALDH2^2/ALDH2^2$ genotypes among 47 subjects were 8.5, 61.7 and 29.8% respectively. The frequency of micronuclei induced by acetaldehyde increased in a dose dependent manner for $ALDH2^1/ALDH2^2$ and $ALDH2^2/ALDH2^2$ genotypes, but no increase was found $ALDH2^1/ALDH2^1$ genotype($p<0.01$). The frequency of micronuclei $ALDH2^1/ALDH2^1$ genotype was lower than those for $ALDH2^1/ALDH2^2$ and $ALDH2^2/ALDH2^2$ genotypes. A significant association was observed between ALDH2 genotypes and facial flushing after alcohol intake ($p<0.05$). Above results suggested a significant association of ALDH2 polymorphism with acetaldehyde-induced micronuclei and facial flushing after alcohol intake.

92 **ROLE OF DNA POLYMERASE ETA IN CISPLATIN- AND UV-INDUCED *IN VIVO* MUTAGENESIS AT THE HUMAN HPRT LOCUS.** King NM[1], Bassett E[2], Bryant MF[1], Chaney SG[2], Cordeiro-Stone M[1]. [1]Department of Pathology and Laboratory Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599. [2]Department of Biochemistry and Biophysics, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599.

DNA polymerase eta catalyzes translesion synthesis of UV-induced DNA lesions. Mutations in the gene encoding polymerase eta *(hRad30A)* result in the variant form of xeroderma pigmentosum (XPV), which is a disease characterized by a high incidence of sunlight-induced skin cancers. Pol eta has also been shown to replicate efficiently through cisplatin adducts *in vitro*. In order to understand the mechanisms of mutagenicity of this widely used chemotherapeutic agent, we sought to determine whether pol eta is a major contributor to replication past cisplatin adducts in intact cells. We compared mutant frequencies at the human hypoxanthine-guanine phosphoribosyl transferase (HPRT) locus in telomerase-immortalized normal and XPV (pol eta-mutant) fibroblasts exposed to cisplatin or UVC. Mutant frequency, based on colony formation in the presence of the purine analog 6-thioguanine, increased in a dose-dependent manner in both cell lines for UVC and cisplatin. In XPV cells, the average mutant frequency was 4.3-fold higher than in normal cells, when both cell lines were treated with $4J/m^2$ UVC. Conversely, 20 and 25 uM cisplatin induced similar mutant frequencies in both cell lines. These results suggest that pol eta is not an essential polymerase for translesion synthesis of cisplatin adducts in human fibroblasts. Using the HPRT assay and a XPV cell line with regulated expression of pol eta, we are currently measuring the effect of this polymerase on both spontaneous and induced mutant frequencies. Supported by PHS awards CA55065 (MCS) and CA8440 (SGC). NMK is supported by the Curriculum in Toxicology Training Grant T32-ES07126.